50. The hybrid enzyme according to claim 19, in which the peptide has the amino acid sequence of SEQ ID NO: 46.

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51. The hybrid enzyme according to claim 19, in which the peptide has the amino acid sequence of SEQ ID NO: 50.--

REMARKS

Claims 1-46 are pending in the application, claims 1-13 and 20-46 stand withdrawn from consideration and claims 14-19 stand rejected. In the present amendment, Applicants have cancelled claims 17 and 18. Applicants have amended claims 14 and 19 as indicated above. Applicants have also added new claims 47-51, which are directed to the peptides that are introduced into the glucose-6-phosphate dehydrogenase. Support for these amendments are found throughout the application. New claim 47 is supported at, e.g., page 12, lines 9-18. New claim 48 is supported at, e.g., page 4, line 15-16. New claim 49 is supported at, e.g., page 4, line 20-22. New claim 50 is supported at, e.g., page 43, line 24 to page 44, line 1 (Example 21). New claim 51 is supported at, e.g., page 44, line 16-18 (Example 22). Thus, no new matter has been added.

Attached hereto is a marked-up version of the changes made to the claims by the current amendment. The attached page is entitled "VERSIONS WITH MARKINGS TO SHOW CHANGES MADE."

Claims 14-19 stand rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. Applicants respectfully traverse this rejection.

The Examiner' admits that the application contains sufficient written description of the species shown in Table 2, i.e., G6PDH enzyme designated as being modified at Asp294/Ser295, Leu305/Asp306, Asp306/Va1307, Pro308/A1a309, A1a309/Asp310, Glu362/Gln363, and C-terminal, in which a peptide of amino acid sequence SEQ ID NO: 2 is inserted at the designated position of a G6PDH enzyme consisting of the amino acid sequence of SEQ ID NO: 6. However, it is the Examiner's position that the specification fails to sufficiently describe any hybrid enzyme of any amino acid sequence and structure having any enzymatic activity in which any peptide is inserted at any position of the amino acid sequence of any glucose-6-phosphate dehydrogenase (G6PDH) of any amino acid sequence, as claimed.

Applicants respectfully disagree with the Examiner's position that the specification describes only the insertion of the peptide having the amino acid sequence of SEQ ID NO: 2 at Asp294/Ser295, Leu305/Asp306, Asp306/Va1307, Pro308/A1a309, A1a309/Asp310, Glu362/G1n363, and C-terminal. Applicants respectfully submit that the specification also describes insertion at the N-terminal (see e.g., page 6, line 5; page 20, line 20-21 and Ex. 17 at page 38). The specification also teaches the insertion of CRP peptides having the amino acid sequence of SEQ ID NO: 1 and SEQ ID NOs: 3-5 (see e.g., Example 1-7 and page 19, line 23-25 and page 20, line 4-8). Furthermore, the specification also describes the insertion of the preS2 peptide (SEQ ID NO: 46, Example 21) and PTH peptide (SEQ ID NO: 50, Example 22) at Asp306/Val307 of G6PDH.

Furthermore, all the Examples demonstrate the basic principle of the invention, that all of the hybrid enzymes obtained in the present application have the same effect although the peptides that are inserted at a specific portion of the G6PDH have no structural relationship with each other. For example, the inserted proteins (e.g., portions of CRP (C1, C2, C3, C5, C13, C15, C18), an antigen portion (preS2) of B-type

hepatitis virus, and a portion of subthyroid hormone have no structural relationship. Thus, the examples clearly show that the hybrid enzymes of the present invention are effective for use in assays for measuring a macromolecule material, regardless of the peptide that is inserted, as long as the peptide is inserted at the specifically claimed portions of the G6PDH protein.

Thus, there is sufficient description to show one of ordinary skill in the art that the inventors had possession of the hybrid enzymes that are claimed.

However, in order to expedite allowance of this application, claim 14 has been amended to limit the G6PDH to that of sequence ID NO. 6 and limit the points of insertion/substitution. Claim 14 has been amended to incorporate claim 17, which recites the positions of insertion, and claim 17 has been canceled.

In light of the present amendments, Applicants respectfully request reconsideration and withdrawal of this rejection.

Claims 14-19 stand rejected under 35 U.S.C. 112, first paragraph, as lacking enablement. The Examiner admits that the specification is enabling for modified G6PDH enzymes (consisting of the amino acid sequence of SEQ ID NO: 6) listed in Table 2 of the specification, i.e., G6PDH enzymes modified at Asp294/Ser295, Leu305/Asp306, Asp306/Val307, Pro308/A1a309, Ala309/Asp310, Glu362/Gln363, and C-terminal, with a peptide of amino acid sequence SEQ ID NO: 2. It is the Examiner's position, however, that it would require undue experimentation to make any hybrid enzyme of any amino acid sequence and structure having any enzymatic activity in which any peptide is inserted at any position of the amino acid sequence of any glucose-6-phosphate dehydrogenase (G6PDH) of any amino acid sequence, wherein when said peptide binds to any material having binding ability to the peptide the activity of any glucose-6-phosphate dehydrogenase is then modulated, and the amino acid sequence of any said peptide to

be inserted in any position, as presently claimed. Applicants respectfully traverse the rejection.

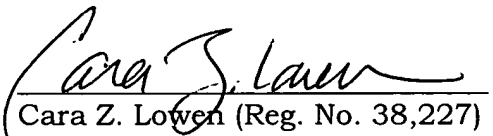
Applicants respectfully submit that, for the reasons stated above, the specification provides enough guidance to enable one of ordinary skill in the art to practice the invention. However, in order to expedite examination and allowance of this application applicants have amended the claims as indicated. In light of the present amendments, Applicants respectfully request reconsideration and withdrawal of this rejection.

In view of the above amendments, it is respectfully submitted that the present application is now in condition for allowance. An early reconsideration and notice of allowance are earnestly solicited.

Should the Examiner wish to discuss the above amendment made herein, the undersigned attorney would appreciate the opportunity to do so. Thus the Examiner is hereby invited to call the undersigned, collect at the number shown below.

Respectfully submitted,

Date: April 29, 2003



Cara Z. Lowen (Reg. No. 38,227)
EDWARDS & ANGELL, LLP
P.O. Box 9169
Boston, MA 02209
Tel: (617) 439-4444

VERSION WITH MARKINGS TO SHOW CHANGES MADE

Please amend the subject application as follows:

IN THE CLAIMS:

Please amend the claims as follows:

14. (amended) A hybrid enzyme having a peptide introduced into a specific position of a glucose-6-phosphate dehydrogenase by insertion or substitution, in which the specific position is at least one position selected from the group consisting of the position between 294-295, between 302-310, between 362-363, the N-terminal and the C-terminal of the amino acid sequence of glucose-6-phosphate dehydrogenase represented by SEQ ID NO: 6.

Please cancel claims 17 and 18, without prejudice.

19. (amended) The hybrid enzyme according to claim 14, in which the peptide comprises an amino acid sequence having at least 6 or more sequential amino acid residues and has a character that there is a material having binding ability specifically to the part of the hybrid enzyme in which the peptide is substituted or inserted.

Please add the following new claims:

-- 47. The hybrid enzyme according to claim 19, in which the peptide comprises an amino acid residue selected from an amino acid sequence of CRP, IgG, IgA, IgM, C3, C4, β2 microglobulin, albumin, α-fetoprotein, CA19-9, prostatic specific antigen, carcinoembryonic antigen, insulin, human chorionic gonadotropin, prolactin,

parathyroid hormone, thyroid stimulating hormone, streptolysin O, hepatitis B virus, hepatitis C virus, human immunodeficiency virus or human papilloma virus.

48. The hybrid enzyme according to claim 19, in which the peptide comprises sequential amino acid residues selected from the amino acid sequence of SEQ ID NO:1.

49. The hybrid enzyme according to claim 19, in which the peptide is selected from the peptides having the amino acid sequences of SEQ ID NO: 2 though SEQ ID NO: 5.

50. The hybrid enzyme according to claim 19, in which the peptide has the amino acid sequence of SEQ ID NO: 46.

51. The hybrid enzyme according to claim 19, in which the peptide has the amino acid sequence of SEQ ID NO: 50.--